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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,842	02/27/2004	Thomas P. Monath	06132/065003	8486
21559	7590	07/20/2006	EXAMINER	
CLARK & ELBING LLP 101 FEDERAL STREET BOSTON, MA 02110			CHEN, STACY BROWN	
			ART UNIT	PAPER NUMBER
			1648	

DATE MAILED: 07/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/789,842	<b>Applicant(s)</b> MONATH ET AL.	
	<b>Examiner</b> Stacy B. Chen	<b>Art Unit</b> 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 15 May 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 1-4 and 8-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 5-7 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 February 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>2/18/05</u> <u>7/28/04</u> . | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Applicant's election without traverse of Group II, claims 5-9, with regard to species Japanese encephalitis virus as the second virus in the claimed chimeric construct, is acknowledged. Claims 1-4 and 8-24 are withdrawn from consideration, being drawn to non-elected subject matter. Therefore, the restriction requirement is deemed proper and made FINAL. Claims 5-7 are under examination.

### ***Claims Summary and Interpretation***

The claims are drawn to a chimeric flavivirus comprising a hinge region mutation in the flavivirus that attenuates the flavivirus. The chimeric flavivirus comprises:

- the capsid and non-structural proteins of a first flavivirus and
- the pre-membrane (PrM) and envelope proteins of a second flavivirus, wherein the envelope protein mutation attenuates the chimeric virus.

Specifically, the second flavivirus is a Japanese encephalitis virus (JEV).

### ***Oath/Declaration***

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

The city of the residence of inventor Juan Arroyo has been altered but not initialed.

***Claim Objections***

Claims 5-7 are objected to for depending from rejected claims. Claim 5 should be rewritten in independent form.

***Claim Rejections - 35 USC § 112***

Claims 5-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims encompass a large genus of flavivirus chimeras, for which Applicant has not demonstrated adequate possession. The embodiments that are adequately described are chimeras having the E279 reversion on Japanese encephalitis, and the substitution of lysine position 202 or 204 of Dengue virus.

The issue at hand is whether the specification provides adequate written description for the genus of mutations encompassed by the claimed chimeric viruses. The genus of mutations includes any sort of mutation within the yellow fever virus envelope region of amino acids 48-61, 127-131 and 196-283. The specification has only described a single substitution at amino acid positions 202 or 204 of Dengue envelope that resulted in a chimeric virus that had the ability to reduce viscerotropism. These two mutations are not representative of the large genus of mutations encompassed by the claims.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or

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chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Applicant has provided a region where the mutation may be made: the hinge region of the yellow fever virus (aa 48-61, 127-131 and 196-283); or amino acids 202 or 204 of Dengue envelope protein. Given that Applicant has not provided a core structure for the mutation, or a nexus between the structure of the mutation and the claimed function (reduces viscerotropism), one of skill in the art is not put in possession of the large genus of mutations encompassed by the claims.

While one of skill in the art could test a plethora of mutations, the statute requires that the specification contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention. Specifically, the specification must contain subject matter that was described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

If Applicant intends for one to test different mutations to discover which ones are suitable, then Applicant has not demonstrated possession of those mutations. The need for further discovery indicates that written description is not satisfied. If Applicant had provided a core structure for the mutation that correlates with the claimed function, then the identification of further mutations would not be unreasonable. However, the specification only provides a general region of amino acids with which one of skill in the art may test different mutations

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(deletion, substitution, or addition of any of the 20 amino acids, any number of amino acids, at any location in the claimed regions). Applicant's specification provides a method for searching for mutations, but appears to attempt to reach-through to the end-products of that method. The specification does not provide for the large genus of chimeric viruses claimed. Regardless of the structure of the envelope hinge region, the specification fails to provide adequate description for the genus of chimeric viruses claimed. Knowing the structure of the hinge region does not make up for not knowing which mutations are acceptable.

Therefore, the claims are rejected as lacking support in the specification for the large genus of viruses encompassed.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5-7 are rejected under 35 U.S.C. 102(b) as being anticipated by "Chambers" (*J. Virology*, 1999, 73(4):3095-3101). The claims are summarized above. Chambers discloses the production of a chimeric yellow fever/Japanese encephalitis virus comprising structural proteins prM and E of JEV within the backbone of a molecular clone YF17D (abstract). The yellow fever virus background naturally comprises capsid and non-structural proteins. The JEV envelope region has a mutation (*i.e.*, reversion) at position 279 in the hinge region (see Tables 3-4). Therefore, the disclosure of Chambers anticipates the invention as claimed.

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Claims 5-7 are rejected under 35 U.S.C. 102(b) as being anticipated by “Arroyo” (J. Virology, 2001, 75(2):934-942). The claims are summarized above. Arroyo discloses a yellow fever virus/Japanese encephalitis virus chimera comprising a yellow fever virus vaccine strain/JEV Nakayama flavivirus having a lysine at position 279 in the hinge region (Table 2). Therefore, the disclosure of Arroyo anticipates the invention as claimed.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 5 and 6 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2 and 4 of copending Application No. 10/345,036. Although the conflicting claims are not identical, they are not patentably distinct

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from each other because the copending claims are directed to a species of the instantly claimed genus.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Conclusion***

No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

*Stacy B. Chen 7/17/06*

**STACY B. CHEN  
PRIMARY EXAMINER**